[Billing Code 4140-01-P]

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Government-Owned Inventions; Availability for Licensing

AGENCY: National Institutes of Health, Public Health Service, HHS

ACTION: Notice

SUMMARY: The inventions listed below are owned by an agency of the U.S. Government and are available for licensing in the U.S. in accordance with 35 U.S.C. 207 to achieve expeditious commercialization of results of federally-funded research and development. Foreign patent applications are filed on selected inventions to extend market coverage for companies and may also be available for licensing.

FOR FURTHER INFORMATION: Licensing information and copies of the U.S. patent applications listed below may be obtained by writing to the indicated licensing contact at the Office of Technology Transfer, National Institutes of Health, 6011 Executive Boulevard, Suite 325, Rockville, Maryland 20852-3804; telephone: 301-496-7057; fax: 301-402-0220. A signed Confidential Disclosure Agreement will be required to receive copies of the patent applications.

Mouse Monoclonal Antibody Targeting Human NOX1, a Target for Cancer and Inflammation

Description of Technology: Available for licensing is a mouse monoclonal antibodies targeting human nicotinamide adenine dinucleotide phosphate-oxidase (NAPH) oxidase 1 (NOX1) enzyme. NOX mediates the homeostasis of reactive oxygen species, which play a critical regulatory role in cancer cell signal transduction and tumor cell differentiation. NOX1-generated hydrogen peroxide can trigger an "angiogenic switch" that includes the induction of angiogenic factors that promote tumor cell vascularization. Additionally, NOX1 may play a role in inflammation.

Investigators at the National Cancer Institute found NOX1 is significantly expressed more in colon and gastric cancers compared with adjacent normal bowel and gastric mucosa respectively. To the best of NIH's knowledge, this is the only monoclonal antibody that can be used to detect human NOX1. This antibody detects endogenous levels of the NOX1 protein and could potentially be used in biochemical laboratory studies as well as diagnostic tests that involve the functional significance of NOX1 in human physiology and pathophysiology, particularly its role in cancer and inflammation.

Potential Commercial Applications:

• Research tool to study cancer and inflammation

• Method to diagnose colon and gastric cancer

• Treatment for cancer and inflammation

Competitive Advantages: To the best of NIH's knowledge, this is the only available monoclonal antibody to detect human NOX1.

Development Stage:

• Early-stage

• In vitro data available

Inventors: James Doroshaw, Krishnendu Roy, Guojian Jiang, Jiamo Lu, and Smitha Antony (all of NCI)

Intellectual Property: HHS Reference No. E-097-2012/0 — Research Tool. Patent protection is not being pursued for this technology.

Licensing Contact: Sabarni K. Chatterjee, Ph.D.; 301-435-5587; chatterjeesa@mail.nih.gov

A Non-invasive Post-treatment Strategy for Stroke by Intranasal Delivery of Cocaine- and Amphetamine-regulated Transcript (CART)

Description of Technology: Cocaine and amphetamine-regulated transcript (CART) is a neuropeptide known to protect against ischemic brain injury when administered before the onset of stroke in mice, both in vivo and in vitro. Utilizing a classic stroke model in rodents, middle cerebral artery occlusion (MCAo), inventors at NIDA discovered a novel post-stroke therapeutic approach involving the intranasal administration of CART. This new non-invasive treatment strategy for stroke patients is effective when initiated three days after stroke, providing a longer treatment window. Nasal delivery of CART improved behavioral recovery and reduced neurological scores in stroke animals. CART, given after stroke, modifies endogenous neural repair in stroke brain by facilitating neuroprogenitor cell proliferation and migration, enhancing reinnervation, and improving the functional recovery.

Potential Commercial Applications: Method of treating stroke

Competitive Advantages:

• New treatment strategy for stroke patients

• Non-invasive (nasal spray)

• Longer treatment window (3 days post-stroke)

• Current strategies aim to protect lesion site from damage, whereas this method helps brain repair

Development Stage:

• Early-stage

• Pre-clinical

• In vitro data available

• In vivo data available (animal)

Inventors: Yun Wang, Hui Shen, Seong Jin Yu, Yihong Yang (all of NIDA)

Publications: Manuscript in preparation

Intellectual Property: HHS Reference No. E-058-2012/0 — U.S. Provisional Application No. 61/592,761 filed 31 Jan 2012

Licensing Contact: Betty B. Tong, Ph.D.; 301-594-6565; tongb@mail.nih.gov

Chimeric Antigen Receptors that Recognize BCMA/ CD269 for Treating Multiple Myeloma

Description of Technology: Available for licensing are chimeric antigen receptors (CARs) that specifically target B-cell maturation antigen (BCMA, CD269), a protein that is highly expressed on the surface of multiple myeloma cells. Multiple myeloma is a malignancy of plasma cells. It is almost always incurable.

A CAR is a fusion protein that can recognize a specific protein on a tumor cell and activate an adaptive immune response to attack the tumor cell. When cultured with multiple myeloma cells in vitro, T-cells engineered to express the CARs were able to induce cell death in the myeloma cells. CARs currently are being evaluated in clinical trials as a promising new area of cancer therapy. The technology available for licensing includes vectors incorporating the CARs, as well as methods of destroying multiple myeloma cells using T-cells engineered to express a CAR.

Potential Commercial Applications:

• Development of a tumor-specific T-cell treatment for multiple myeloma

• Development of a tumor-specific T-cell treatment for Hodgkin's lymphoma

• Treatment of diseases associated with increased or preferential expression of BCMA/ CD269

Competitive Advantages:

• Specifically targets an antigen that is highly expressed in tumor cells of multiple myeloma and Hodgkin's lymphoma

• Amenable for adoptive transfer approaches

• No other anti-BCMA immunotherapies are in clinical trials

• Targeted therapy decreases non-specific killing of healthy, essential cells, resulting in fewer non-specific side-effects and healthier patients

Development Stage:

• Pre-clinical

• Clinical

• In vitro data available

Inventor: James N. Kochenderfer (NCI)

Intellectual Property: HHS Reference No. E-040-2012/0 — U.S. Provisional Application 61/622,600 filed 11 April 2012

Related Technologies:

• HHS Reference No. E-205-2009/0 — Treating Cancer with Anti-angiogenic Chimeric Antigen Receptors

• HHS Reference No. E-148-2011/0 — Breakthrough Immunotherapy for Brain Cancer: Epidermal Growth Factor Receptor Variant III Chimeric Antigen Receptors

• HHS Reference No. E-086-2006/0 — Hybrid T-Cell Receptors for the Development of Improved Vaccines

• HHS Reference No. E-265-2011/0 — Chimeric Antigen Receptors to CD22 for Treating Hematological Cancers

Licensing Contact: Patrick McCue, Ph.D.; 301-435-5560; mccuepat@mail.nih.gov

Collaborative Research Opportunity: The National Cancer Institute, Experimental Transplantation and Immunology Branch, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize chimeric antigen receptors to genetically-modify T cells to recognize BCMA/ CD269. For collaboration opportunities, please contact John Hewes, Ph.D. at hewesj@mail.nih.gov.

ROCK Inhibitors for the Prevention of Breast Cancer Metastasis and Tumor Relapse

Description of Technology: The recent success of therapeutic approaches has significantly reduced breast cancer mortality, however, breast cancers that are diagnosed as "triple-negative" (lacking the estrogen receptors, HER2/Neu, and progesterone receptors) don't respond to these available therapies and some hormone receptor or NER2/Neu-positive breast cancers have shown a resistance to these treatments. These breast cancers account for nearly 90% of all breast cancer deaths. Therefore, examining the mechanisms by which the breast cancer cells spread from their primary sites to distant organs is an active area of research. The NIH inventors have discovered that by blocking a key biochemical route necessary for the egress of breast cancer cells into circulation, the CXCR4-Galpha13-Rho signaling pathway, they can prevent the dissemination of breast cancer cells and thereby prevent breast cancer metastasis. In particular, they have discovered that ROCK inhibitors, such as Fasudil, can be used to treat of breast cancer patients after the initial clinical intervention (i.e., surgery, radiation, chemo-radiation, or their combination) to delay or prevent patient relapse due to the metastasis of any residual or prior undetected breast cancer cells.

Potential Commercial Applications:

• Treatment of "triple-negative" breast cancers.

• Treatment of hormone receptor or NER2/Neu-positive breast cancers that are resistant to currently available therapies.

Competitive Advantages: ROCK inhibitors can delay or prevent breast cancer metastasis in patients where there are no effective therapies currently available.

Development Stage:

• Pre-clinical

• In vitro data available

• In vivo data available (animal)

Inventors: Silvio Gutkind and Alfredo Molinolo (NIDCR)

Intellectual Property: HHS Reference No. E-280-2011/0 — U.S. Application No. 61/536,434 filed 19 Sep 2011

Licensing Contact: Whitney Hastings; 301-451-7337; hastingw@mail.nih.gov

Cell Line for Producing Furin That Can Cleave Papillomavirus L2, Toxins and Other Substrates

Description of Technology: Human papillomavirus (HPV) is an infectious agent that is responsible for several different diseases. Although HPV often manifests as warts, it can also result in certain types of cancer. Since HPV can remain latent for long periods of time, the disease can be transmitted by someone who is not aware they are contagious. This partially explains why HPV is the most common sexually transmitted disease. The HPV genome consists of several genes, including the two late-expressed genes known as L1 and L2. The HPV L1 and HPV L2 genes encapsulate amplified HPV genomes prior to their release in virions, which infect other cells. Since HPV L2 is present on the HPV virion when it is released from a cell, people infected with HPV will generate an immune response against HPV L2 to help contain the infection. This includes the generation of neutralizing antibodies against HPV L2. By examining a sample for the presence of these neutralizing antibodies, it can be determined whether a patient has HPV and is capable of spreading the disease.

This technology describes a Chinese Hamster Ovary (CHO) cell line which expresses a truncated version of mouse furin which retains activity. Furin is an enzyme that cleaves proteins at a specific, defined amino acid sequence. The cleavage of HPV L2 makes it more susceptible to detection by neutralizing antibodies. As a result, the cell line can increase the sensitivity of an assay for detecting neutralizing antibodies to HPV L2.

Potential Commercial Applications:

• The cell line secretes a truncated mouse furin for use in any assays which benefit from furin activity.

• A specific use for the cell line is testing samples for neutralizing antibodies to HPV L2.

• The cells can be developed into a validated assay for detecting neutralizing antibodies to HPV L2 as a means of diagnosing HPV infection.

Competitive Advantages:

• Neutralizing antibodies to HPV L2 are more readily detected when the protein is first cleaved by furin.

• The cell lines represent an established and efficient research tool for cleaving HPV L2 for more efficient detection of neutralizing antibodies to the protein.

• An assay for detecting HPV infection can be useful for detecting those who are asymptomatic, which is common with HPV infections.

Development Stage: In vitro data available

Inventors: David FitzGerald et al. (NCI)

Publications:

1. Chiron MF, et al. Furin-mediated cleavage of Pseudomonas exotoxin-derived chimeric toxins. J Biol Chem. 1997 Dec 12;272(50):31707-11. [PMID 9395513]

2. Richards RM, et al. Cleavage of the papillomavirus minor capsid protein, L2, at a furin consensus site is necessary for infection. Proc Natl Acad Sci U S A. 2006 Jan 31;103(5):1522-7. [PMID 16432208]

3. Day PM, Schiller JT. The role of furin in papillomavirus infection. Future Microbiol. 2009 Dec;4(10):1255-62. Review. [PMID 19995186]

Intellectual Property: HHS Reference No. E-233-2011/0 — Research Tool. Patent protection is not being pursued for this technology.

Licensing Contact: David A. Lambertson, Ph.D.; 301-435-4632; lambertsond@mail.nih.gov

Novel Reduced Toxicity Tropolone Derivative Compounds That Have Anti-Viral Activity Through Inhibiting RNase H Activity

Description of Technology: Several novel tropolone derivatives have been identified that inhibit HIV-1 RNase H function and have potential for anti-viral activity due to reduced cellular toxicity. Inhibiting RNase H function is a potential treatment for many viral infections, since RNase H function is essential for viral replication for many pathogenic retroviruses such as HIV-1 and HIV-2. Although many hydroxytropolone compounds are potent RNase H inhibitors biding at the enzymatic active site, they are limited as therapeutic candidates by their toxicity in mammalian cells. The toxicity thought to be a result of inhibition of multiple essential mammalian metalloenzymes. We reasoned that the potential beneficial application of tropolone RNase H inhibition might

be of therapeutic use if the toxic effects in mammalian cell were eliminated. By selectively adding steric bulk to add new drug-enzyme contacts for the RNase H active site, a number of novel compounds, that have initially demonstrated reduced cytotoxicity, have been produced. Importantly, these novel compounds appear to retain antiviral activity essential for use as therapeutics.

Potential Commercial Applications: Anti-viral therapeutic: HIV-1 and other RNase H-dependent viral infections

Competitive Advantages:

• Potentially reduced toxicity

• Availability of x ray crystallographic information to guide analog design

Development Stage:

• Pre-clinical

• In vitro data available

Inventors: John Beutler, Suhman Chung, Stuart F. LeGrice, Jennifer A. Wilson (NCI); Craig J. Thomas and Jian-kang Jiang (NCATS)

Publications:

1. Chung S, et al. Synthesis, activity and structural analysis of novel alpha-hydroxytropolone inhibitors of human immunodeficiency virus reverse transcriptase-associated ribonuclease H. J Med Chem 2011 Jul 14;54(13):4462-4473. [PMID 21568335]

2. Budihas SR, et al. Selective inhibition of HIV-1 reverse transcriptase-associated ribonuclease H activity by hydroxylated tropolones. Nucl Acids Res 2005 33 (4):1249-1256. [PMID 15741178]

Intellectual Property: HHS Reference No. E-081-2011/0 — U.S. Provisional Application No. 61/484,779 filed 11 May 2011

Licensing Contact: Edward "Tedd" Fenn, J.D.; 301-435-5031; fenned@mail.nih.gov

Collaborative Research Opportunity: The Molecular Targets Laboratory, National Cancer Institute, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize antiviral tropolone derivatives developed by systematic medicinal chemistry on the lead series. For collaboration opportunities, please contact John Hewes, Ph.D. at hewesj@mail.nih.gov.

Hspa2 Knockout Mice for Study of Spermatogenesis and Male Infertility

Description of Technology: HSPA2 is a member of the HSP70 family of heat-shock proteins that serve as molecular chaperones. Researchers discovered that HSPA2 protein is expressed in spermatogenesis during the meiotic phase. Spermatogenic cells lacking the HSPA2 protein arrest in mid-meiosis and undergo apoptosis. HSPA2 is present in the synaptonemal complex of wild-type mice and the chromosomes fail to separate in HSPA2-deficient mice (previously known as Hsp70-2-/- mice), suggesting that HSPA2 is required for the chromosomal events of meiosis such as synapsis, crossing over, or recombination.

Researchers at NIEHS developed a knockout strain of mice in which the heat shock protein gene (Hspa2) is disrupted. This mouse model is useful in studying the

process of spermatogenesis and the influence of various environmental toxins or drugs on sperm production and male infertility.

Potential Commercial Applications:

• Mouse model to study spermatogenesis and male infertility

• Mouse model to study meiosis or the roles of heat-shock proteins in general

• Mouse model to evaluate effects of meiosis-disrupting agents on meiotic recombination and generation of mutations transmitted to offspring

Development Stage:

• In vitro data available

• In vivo data available (animal)

Inventor: Edward M. Eddy (NIEHS)

Publication: Dix DJ, et al. Targeted gene disruption of Hsp70-2 results in failed meiosis, germ cell apoptosis, and male infertility. Proc Natl Acad Sci USA. 1996 Apr 93(8):3264-3268. [PMID 8622925]

Intellectual Property: HHS Reference No. E-052-2011/0 — Research Tool. Patent protection is not being pursued for this technology.

Related Technology: HHS Reference No. E-290-2011/0 — Research Tool (Transgenic Hspa2-Cre Mice for Studying Spermatogenesis and Male Infertility). Patent protection is not being pursued for this technology.

Licensing Contact: Lauren Nguyen-Antczak, Ph.D., J.D.; 301-435-4074; Lauren.Nguyen-Antczak@nih.gov

Collaborative Research Opportunity: The NIEHS is seeking statements of capability or interest from parties interested in collaborative research to further develop,

evaluate or commercialize this mouse strain. For collaboration opportunities, please contact Elizabeth Denholm, Ph.D. at denholme@niehs.nih.gov.

Transgenic Hspa2-Cre Mice for Studying Spermatogenesis and Male Infertility

Description of Technology: HSPA2 is a member of the HSP70 family of heat-shock proteins that serve as molecular chaperones. Hspa2-cre expression mimics the spermatogenic cell-specific expression of endogenous HSPA2 within the testis, being first observed in leptotene/zygotene spermatocytes. Expression of the transgene is also detected at restricted sites in the brain, as occurs for endogenous HSPA2.

Researchers at NIEHS developed the first transgenic mouse line that expresses Cre-recombinase under the control of the promoter of the heat shock protein A2 (Hspa2) gene. Expression of the Hspa2-Cre transgene during meiosis in male germ cells makes these mice a useful tool for defining the roles of genes expressed at different times during spermatogenesis or expressed in spermatogenic cells.

Potential Commercial Applications:

• New mouse model to study spermatogenesis and male infertility

• New mouse model to study meiosis or the roles of heat-shock proteins in general

Competitive Advantages: Researchers generated an Hspa2-cre line that expresses cre in spermatocytes to overcome the limitations of other transgenic lines.

Development Stage:

• In vitro data available

• In vivo data available (animal)

Inventor: Edward M. Eddy (NIEHS)

Publication: Inselman AL, et al. Heat shock protein 2 promoter drives cre expression in spermatocytes of transgenic mice. Genesis. 2010 Feb 48(2):114-120. [PMID 20027617]

Intellectual Property: HHS Reference No. E-290-2011/0 — Research Tool. Patent protection is not being pursued for this technology.

Related Technology: HHS Reference No. E-052-2011/0 — Research Tool (Hspa2 Knockout Mice for Study of Spermatogenesis and Male Infertility). Patent protection is not being pursued for this technology.

Licensing Contact: Lauren Nguyen-Antczak, Ph.D., J.D.; 301-435-4074; Lauren.Nguyen-Antczak@nih.gov

Collaborative Research Opportunity: The NIEHS is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize this mouse strain. For collaboration opportunities, please contact Elizabeth Denholm, Ph.D. at denholme@niehs.nih.gov.

Diagnostic H5N1 Avian Influenza Virus Peptides

Description of Technology: The recent spread of highly pathogenic H5N1 avian influenza viruses among poultry and transmission of these viruses to humans raises concerns of a potential influenza pandemic. There is a need to track the spread of these viruses both in the animal and human populations to avert or reduce the impact of any potential influenza pandemic as well as to know the actual number (accurate surveillance) of people infected with H5N1, including individuals with subclinical H5N1 infection.

The subject technology is a specific combination of H5N1 peptides useful for assays to detect antibodies generated against a wide range of different H5N1 strains. The combination of peptides was able to specifically detect anti-H5N1 antibodies from serum samples of H5N1 survivors at early and later times post infection while excluding antibodies generated in individuals infected with other strains of influenza virus. Also, the peptides did not react with sera from individuals vaccinated with H5N1 vaccine, in contrast to the strain-specific detection of anti-H5N1 antibodies in sera from infected individuals. Immunoassays using the H5N1 peptide combination provide highly specific, sensitive and reproducible methods for diagnosing H5N1 infection in humans and animals.

Potential Commercial Applications: Diagnostics for influenza virus specific antibodies in humans and animals.

Competitive Advantages: High specificity, sensitivity, and reproducibility

Development Stage:

• Pre-clinical

• In vitro data available

Inventors: Hana Golding and Surender Khurana (FDA)

Publication: Khurana S, et al. H5N1-SeroDetect EIA and rapid test: a novel differential diagnostic assay for serodiagnosis of H5N1 infections and surveillance. J Virol. 2011 Dec;85(23):12455-63. [PMID 21957281]

Patent Status: HHS Reference No. E-093-2010/0 — PCT Application No. PCT/US2011/032555 filed 14 Apr 2011, which published as WO 2011/130555 on 20 Oct 2011

Related Technology: HHS Reference No. E-236-2007/3 — U.S. Patent Application No. 12/664,052 filed 10 Dec 2009

Licensing Contact: Kevin W. Chang, Ph.D.; 301-435-5018; changke@mail.nih.gov

Parvovirus B19 Codon Optimized Structural Proteins for Vaccine and Diagnostic Applications

Description of Technology: Parvovirus B19 (B19V) is the only known pathogenic human parvovirus. Infection by this viral pathogen can cause transient aplastic crisis in individuals with high red cell turnover, pure red cell aplasia in immunosuppressed patients, and hydrops fetalis during pregnancy. In children, B19V most commonly causes erythema infectiosum, or fifth's disease. Infection can also cause arthropathy and arthralgia. The virus is very erythrotropic, targeting human erythroid (red blood) progenitors found in the blood, bone marrow, and fetal liver. Currently, there are no approved vaccines or antiviral drugs for the treatment or prevention of B19V infection.

The subject technology is a series of plasmid constructs with codon optimized B19 viral capsid genes (VP1 and VP2) that can be expressed in mammalian cells. Transfection of vectors encoding these optimized VP1 and VP2 genes into different mammalian cell lines, including 293, Cos7, and Hela cells produce virus-like particles (VLPs). The vectors include bicistronic plasmids expressing the VP1 and VP2 proteins at different ratios to produce B19V VLPs with optimal antigenicity for vaccine

applications. This technology can also be used for diagnostic applications and development of a viral packaging system for producing infectious B19V virus.

Potential Commercial Applications:

• VLPs based vaccines for the prevention and/or treatment of B19V infection

• DNA based vaccines for the prevention and/or treatment of B19V infection

• B19V diagnostics

• Viral packaging system

Competitive Advantages:

• Codon optimized VP1 and VP2 genes for better expression in mammalian cell lines

• Expression of B19V VLPs from "nonpermissive" cell lines

Development Stage: In vitro data available

Inventors: Ning Zhi, Sachiko Kajigaya, and Neal S. Young (NHLBI)

Patent Status: HHS Reference No. E-011-2010/0 — PCT Application No. PCT/US2011/024199 filed 09 Feb 2011, which published as WO 2011/100330 on 22 Dec 2011

Licensing Contact: Kevin W. Chang, Ph.D.; 301-435-5018; changke@mail.nih.gov

Collaborative Research Opportunity: The National Heart Lung and Blood Institute, Hematology Branch, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize the subject technology. Please contact Cecilia Pazman, Ph.D., at pazmance@mail.nih.gov for more information.

Construct for Tetracycline Inducible Podocyte Specific Gene Expression in Mice

Description of Technology: The National Institutes of Health announces the generation of a construct by ligating 2.5kb human podocin promoter sequence to gene encoding reverse tetracycline-controlled transcriptional activator which enables tetracycline-inducible podocyte specific gene of interest expression with another construct consisting of tetracycline responsive element, minimal CMV promoter and gene of interest.

Podocytes are post-mitotic epithelial cells that are positioned on the exterior aspect of the glomerular capillary wall and contribute to the selective molecular permeability of glomeruli. Podocyte damage or dysfunction results in loss of the characteristic foot processes that normally interdigitate and form the selective permeability barriers composed of filtration slits bridged by slit diaphragms. Minimal damage causes proteinuria that in the case of minimal change disease can be reversed by steroid treatment. In focal segmental glomerulosclerosis, more severe loss of podocytes ultimately results in glomerulosclerosis. The podocyte-specific inducible transgene system can be used to identify factors that exacerbate or ameliorate podocyte injury, and can be used to express Cre-recombinase.

Potential Commercial Applications: This technology can be used for the study of renal disease.

Competitive Advantages: The podocyte-specific inducible transgene system can be used to identify factors that exacerbate or ameliorate podocyte injury, and can be used to express Cre-recombinase.

Development Stage: Pre-clinical

Inventors: Jeffrey B. Kopp et al. (NIDDK)

Publication: Shigehara T, et al. Inducible podocyte-specific gene expression in transgenic mice. J Am Soc Nephrol. 2003 Aug;14(8):1998-2003. [PMID 12874453]

Intellectual Property: HHS Reference No. E-299-2007/0 — Research Material. Patent protection has not been pursued for this technology.

[Note: The use of Tetracycline controllable expression systems is covered by a series of patents including US #5,464,758 and 5,814,618 which are proprietary to TET systems GmbH & Co. KG. Interested parties are also advised to contact TET Systems, info@tetsystems.com or by electronic request at www.tetsystems.com/main_inquiry.htm]

Licensing Contact: Fatima Sayyid, M.H.P.M.; 301-435-4521; Fatima.Sayyid@nih.hhs.gov

Parallel High Speed Single Molecule Nucleic Acid Sequencing

Description of Technology: This invention entails a new system, methods, and compositions for DNA sequencing, known as Two Dye Sequencing (TDS). The system utilizes Forster Resonance Energy Transfer (FRET). The TDS method consists of the following steps:

1) Attaching to a microscope chamber, DNA polymerases labeled with a donor fluorophore.

2) Adding to the chamber DNA molecules annealed to a primer.

3) Adding four dNTPs, each labeled with a different fluorescent acceptor dye.

4) Exciting the donor fluorophore with light, causing energy transfer (FRET) to the acceptor fluorophore for a given dNTP, that then radiates light of a different wavelength.

5) Identifying nucleotides as they are added to the nascent polynucleotide by recording the FRET signals at the location of each DNA polymerase in the microscope field of view.

6) Converting the sequential signals into a DNA sequence for each DNA molecule in the microscope field of view.

Potential Commercial Applications: High throughput sequencing of single DNA molecules on a substrate.

Competitive Advantages:

• Detection of individual DNA molecule sequences

• Sequences multiple DNA molecules in parallel with one microscope

• Eliminates washing steps, because all four nucleotides are added at once

• Rapid, works at the speed of the DNA polymerase

Development Stage: Early-stage

Inventors: Thomas D. Schneider and Denise Rubins (NCI)

Intellectual Property: HHS Reference No. E-033-1999/0 —

• US Patent No. 6,982,146 issued 03 Jan 2006

• PCT Application No. PCT/US00/23736 filed 29 Aug 2000

• US Application No. 12/886,686 filed 29 Aug 2000

Related Technologies: HHS Reference No. E-194-2005/0 —

• US Patent No. 7,871,777 issued 18 Jan 2011

• EP Patent No. 1960550 issued 15 Sep 2010, validated in DE, FR, and GB

• JP Application No. 2009-545768 filed 12 Dec 2006

• US Application No. 12/980,802 filed 29 Dec 2010

Licensing Contact: Cristina Thalhammer-Reyero, Ph.D., MBA; 301-435-4507; thalhamc@mail.nih.gov

The Medusa™ Sequencer: A DNA or RNA Sequencing Machine the Size of a Molecule

Description of Technology: Current high-throughput DNA sequencing methods suffer from several limitations. Many methods require multiple fluid handling steps, fixing of molecules on beads or a 2D surface, and provide very short read-lengths. The NIH inventors offer a DNA or RNA sequencing device that drastically simplifies the process by combining all elements for sequence detection in a single molecule, the Medusa™ Sequencer.

The Medusa™ Sequencer utilizes Forster Resonance Energy Transfer (FRET) to read a polynucleotide sequence while synthesizing a complementary strand. The device consists of a DNA (or RNA) polymerase labeled with a FRET donor fluorophore and attached to a set of four flexible arms. The tip of each arm carries a distinct set including one nonhydrolyzable nucleotide and one FRET acceptor fluorophore. While a Medusa™ Sequencer synthesizes a complementary polynucleotide strand, the four different arms continuously "test" the polymerase pocket creating a characteristic FRET signal for the correct nucleotide. The series of FRET signals reveals the unknown polynucleotide sequence.

Potential Commercial Applications:

• High-throughput DNA or RNA sequencing

• Alternative to microarrays for expression analysis

• Diagnostics of genetic diseases

Competitive Advantages:

• Single reagent for synthesis and sequencing

• Eliminates repetitive fluid handling steps

• Able to count single mRNA or DNA molecules

• Exceptionally low manufacturing cost

• Could be injected in living cells to read/count mRNA sequences directly

• Low error rate per base

• High speed; one microscope obtains many sequences in parallel

• Can be 3D-arrayed in a gel for ultra-high density

• Use with Sequence Walkers for diagnostics

(http://alum.mit.edu/www/toms/g863a.html)

Development Stage: Early-stage

Inventors: Thomas D. Schneider, IIya G. Lyakhov, Danielle Needle (NCI)

Publication: The technology is further described at

http://alum.mit.edu/www/toms/patent/medusa.

Intellectual Property: HHS Reference No. E-194-2005/0 —

• US Patent No. 7,871,777 issued 18 Jan 2011

• EP Patent No. 1960550 issued 15 Sep 2010, validated in DE, FR, and GB

• JP Application No. 2009-545768 filed 12 Dec 2006

• US Application No. 12/980,802 filed 29 Dec 2010

Related Technologies:

HHS Reference No. E-195-2005/0 —

• US Application No. 60/749,858 filed 12 Dec 2005

• US Application No. 11/638,160 filed 12 Dec 2006

HHS Reference No. E-033-1999/0 —

• US Patent No. 6,982,146 issued 03 Jan 2006

• PCT Application No. PCT/US00/23736 filed 29 Aug 2000

• US Application No. 12/886,686 filed 29 Aug 2000

Licensing Contact: Cristina Thalhammer-Reyero, Ph.D., MBA; 301-435-4507; thalhamc@mail.nih.gov

Collaborative Research Opportunity: The National Cancer Institute, Gene Regulation and Chromosome Biology Laboratory, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize the Medusa™ Sequencer. For collaboration opportunities, please contact John Hewes, Ph.D. at hewesj@mail.nih.gov.

Nanoprobes for Detection or Modification of Molecules

Description of Technology: This invention describes "Rod-tether Nanoprobes", devices consisting of a rigid molecular rod with a flexible molecular tether attached at both ends that can detect and/or modify molecules. Each tether tip has a functional group, such as an antibody or oligonucleotide that recognizes a target molecule. In addition, one tip carries a donor fluorophore and the other carries an acceptor fluorophore. The

fluorophores form a pair for Forster Resonance Energy Transfer (FRET). In the absence of the target molecule, the rod keeps the tether arms apart, while in the presence of the target molecule, both recognizers bind to the target. This binding holds the donor and acceptor fluorophores close together, allowing a FRET signal. By reducing an ELISA-like assay entirely to the molecular level, complex macroscopic or microfluidic washing and pumping systems can be eliminated. Rod-tether Nanoprobes can detect a wide variety of clinical and biowarfare reagents. The nanoprobes can also rapidly and simply detect, modify, and/or destroy endogenous molecules (e.g., proteins, mRNA) involved in a broad range of diseases. The simplest ssDNA-detecting nanoprobe has been created.

Potential Commercial Applications:

- Instantly detect molecules of interest (e.g., proteins, mRNA) in multiple settings:
  - Clinical
  - Scientific research
  - Biowarfare
- An improved substitute for ELISA assays
- Modify or destroy target molecules, while detecting them
- Detect genetic diseases in the clinic from patient blood samples

Competitive Advantages:

- Only one reagent required for detection
- Entire reaction contained in a single molecule
- Eliminates washing steps
- Complicated and expensive microfluidic chips are eliminated
- High speed

• Exceptionally low cost

Development Stage: Early-stage

Inventors: Thomas D. Schneider, IIya G. Lyakhov, Danielle Needle (NCI)

Publication: The technology is further described at http://alum.mit.edu/www/toms/patent/nanoprobe/.

Intellectual Property: HHS Reference No. E-195-2005/0 —

• US Application No. 60/749,858 filed 12 Dec 2005

• US Application No. 11/638,160 filed 12 Dec 2006

Related Technologies: HHS Reference No. E-194-2005/0 —

• US Patent No. 7,871,777 issued 18 Jan 2011

• EP Patent No. 1960550 issued 15 Sep 2010, validated in DE, FR, and GB

• JP Application No. 2009-545768 filed 12 Dec 2006

• US Application No. 12/980,802 filed 29 Dec 2010

Licensing Contact: Cristina Thalhammer-Reyero, Ph.D., MBA; 301-435-4507; thalhamc@mail.nih.gov

Collaborative Research Opportunity: The National Cancer Institute, Gene Regulation and Chromosome Biology Laboratory, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize Rod-Tether Nanoprobes. For collaboration opportunities, please contact John Hewes, Ph.D. at hewesj@mail.nih.gov.

Immunogenic Peptides (Vaccines) for the Treatment of Prostate and Breast Cancer

Description of Technology: Collectively, cancer is the second leading cause of death in the United States. Current treatments of cancer often involve non-specific strategies (such as chemotherapy) which attack healthy cells as well as diseased cells, leading to harmful side-effects. As a result, the development of more targeted means of treating cancer are highly sought. One option for a targeted treatment is the creation of a vaccine that induces an immune response only against cancer cells. In this sense, vaccination involves the introduction of a peptide into a patient that causes the formation of T cells that recognize the peptide. If those recognize a peptide found in a protein found selectively on cancer cells, those T cells can trigger the death of those cancer cells without harming non-cancer cells. This can result in fewer side effects for the patient. TARP (T cell receptor gamma alternate reading frame protein) is a protein that is selectively expressed on the cells of certain types of prostate and breast cancer. This invention concerns the identification of immunogenic peptides within TARP, and their use to create an anti-cancer immune response in patients. By introducing these peptides into a patient, an immune response against these cancer cells can be initiated by the peptides, resulting in treatment of the cancer. A phase I clinical trial in stage D0 prostate cancer patients is nearing completion. Initial results indicate a statistically significant decrease in the slope of PSA for 48 weeks after vaccination.

Potential Commercial Applications:

• Peptides can be used as cancer vaccines.

• Treatment of any cancer associated with increased or preferential expression of TARP.

• Specific diseases include breast cancer and prostate cancer.

Competitive Advantages: Targeted therapy decreases non-specific killing of healthy, essential cells, resulting in fewer non-specific side-effects and healthier patients.

Development Stage:

• Pre-clinical

• Clinical

• In vivo data available (animal)

• In vivo data available (human)

Publications:

1. Epel M, et al. Targeting TARP, a novel breast and prostate tumor-associated antigen, with T cell receptor-like human recombinant antibodies. Eur J Immunol. 2008 Jun;38(6):1706-1720. [PMID 18446790]

2. Oh S, et al. Human CTLs to wild-type and enhanced epitopes of a novel prostate and breast tumor-associated protein, TARP, lyse human breast cancer cells. Cancer Res. 2004 Apr 1;64(7):2610-2618. [PMID 15059918]

Intellectual Property: HHS Reference No. E-116-2003/0 —

• US Patent 7,541,035 issued 02 Jun 2009

• US Patent 8,043,623 issued 25 Oct 2011

Licensing Contact: David A. Lambertson, Ph.D.; 301-435-4632; lambertsond@mail.nih.gov

Collaborative Research Opportunity: The National Cancer Institute, Vaccine Branch, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize a prostate cancer

vaccine targeting the TARP antigen currently completing phase I clinical trials. For collaboration opportunities, please contact John Hewes, Ph.D. at hewesj@mail.nih.gov.

April 27, 2012
Date

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Richard U. Rodriguez, M.B.A.
Director
Division of Technology Development and Transfer
Office of Technology Transfer
National Institutes of Health

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